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REPORT SUMMARY

FETAL ALCOHOL SYNDROME:

Diagnosis, Epidemiology, Prevention, and Treatment

Committee to Study Fetal Alcohol Syndrome

Division of Biobehavioral Sciences and Mental Disorders

INSTITUTE OF MEDICINE

Kathleen Stratton, Cynthia Howe, and Frederick Battaglia, *Editors*

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This report has been reviewed by a group other than the authors according to procedures approved by a Report Review Committee consisting of members of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine.

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Committee to Study **Fetal Alcohol Syndrome**

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Preface

The last 20 years have brought home to most Americans the profound impact of substance abuse on individuals, their families, and society. Most extended families have had some experience with this problem.

We are only recently becoming more aware of the terrible effects of substance abuse on pregnant women and their unborn children. Of all current substance abuse, alcohol is the most serious problem by far, whether judged by its frequency or by its capacity to injure-the fetus. In its most obvious form, it leads to a constellation of findings in the infant that are referred to as the fetal alcohol syndrome (FAS).

Because of concerns about the magnitude of the problem, the U.S Congress mandated this study, under the auspices of the Institute of Medicine (IOM) of the National Academy of Sciences. From rhe outset, the committee was aware of treading on new ground in addressing alcohol abuse during pregnancy since the approach used in this study might serve as a paradigm for other studies of substance abuse in pregnancy. What are the unique characteristics of alcohol abuse in pregnancy that make it such a challenge for medicine and for society in general?

First, this is not a disease that affects only the child with FAS; it involves both the mother and her baby. FAS is a classic example of a **family problem.** A mother who abuses alcohol needs and deserves treatment for this problem, not only during pregnancy but afterward. If she continues to be alcohol-dependent she may very well die from the disease in a few years and, in the interim, have additional affected pregnancies. Alcohol abuse affects her ability to care properly for her children throughout childhood. The affected child needs continued medical care aimed at minimizing any of the developmental handicaps imposed by FAS. As with many birth defects, optimal care requires coordinated effort from many groups, including providers of health care, social services, and schools.

Secondly, as with many risk factors for a fetus, whether influenced by maternal behavior (e.g., infection with sexually transmitted diseases) or not (e.g., inborn errors of metabolism), if the mother does not receive treatment the effects can be amplified by recurrence, that is by births to that mother of additional affected children, or by the children-when they reach reproductive age-bearing affected infants of their own.

Given these effects of alcohol abuse during pregnancy, the committee addressed the issue of updating the diagnostic criteria that should be used for FAS. We were concerned that, without well-defined criteria, any developmental delay or behavioral abnormality in children whose mothers had any level of alcohol intake might lead to inappropriate labeling with the FAS diagnosis. The criteria recommended are as close as possible to those commonly used by workers in this field and, at the same time, follow the guidelines generally used for setting diagnostic criteria in other areas of medicine.

A consideration of diagnostic criteria brought out the fact that many infants with FAS are not being diagnosed at birth, either because they cannot be or because professionals do not have the tools and training to do so. Pattern recognition is part of the diagnostic criteria in a disease of dysmorphogenesis. In this case it involves recognition of the pattern of facial abnormalities and of the neurobehavioral and developmental characteristics associated with FAS. Who is to be trained for diagnosis in the newborn period, or at any time in childhood? This is an important issue when one considers surveillance approaches that might be applicable on a public health basis. The committee was impressed that this area needs some focused clinical research before widespread surveillance approaches can be recommended. Such research and field testing is considered an urgent priority.

Also relevant to both diagnosis and prevention is the issue of whether there are problems of development or behavior from any alcohol intake, no matter how low, during pregnancy. Since this is not yet known,

the committee focused on the constellation of infant problems for which good evidence exists of a relationship with maternal abuse of alcohol.

There have been excellent reviews of animal studies relating to FAS. For this reason, the report does not include a detailed review of this topic. Animal models have been established, and studies at the levels of integrative physiology and cell biology have contributed substantially to our understanding of some aspects of the disease. The report attempts to place these basic studies in context in terms of their contribution to our understanding of pathogenesis and prevention. For example, basic research contributed to our understanding of FAS by firmly establishing alcohol as a teratogen. It was also important in highlighting those organ systems likely to be most affected during in utero development. In terms of developmental timing, basic research established the important concept that alcohol can injure the fetus, particularly the central nervous system, not only during embryogenesis, but also later in pregnancy. It was clear to the committee that there are many areas in which additional basic research could make substantial contributions to our understanding of the relationship of dosage, developmental timing, genetic susceptibility, gender differences, and differences in tolerance imposed by the endocrine changes of pregnancy. Such research could contribute by pointing toward additional therapeutic approaches that might be used during pregnancy.

The sections on prevention and treatment once again emphasize that two patients must be considered. Treatment of alcohol abuse and dependence in a pregnant woman is also prevention of FAS in her fetus. The committee wrestled with the difficulty that universal prevention methods appear to have an impact on women with low or moderate alcohol intake but no impact on women who abuse alcohol. Yet, it is this latter group that produce infants with FAS and related problems. Thus, targeting specific prevention and treatment approaches to this latter group is vital if we are to reduce the incidence of FAS. Unfortunately, currently there is little evidence of successful approaches. Too often, we have assumed that whatever works in men who abuse alcohol will in women who abuse alcohol. This is another area in which clinical research, with strong evaluation components, needs to be implemented.

Treatment of the child begins whenever FAS (or a related disorder) is recognized. The later this recognition occurs in development, the less success treatment protocols will have. For this reason, training medical staff and other gatekeepers in pattern recognition and appropriate history taking in pregnancy is of paramount importance. As with many birth defects, there is a tendency to assume that the damage is done by the time the infant is born. However, this report brings out the lack of knowledge about how much subsequent developmental difficulty is due to actual organic injury at birth, how much is due to the chaotic environment in which most of these children are raised, and how much could be ameliorated by appropriate postnatal intervention and treatment. Such children should not be "discarded" by society and if, as a society, we are sincere in this belief, then the same multidisciplinary approach to their treatment and schooling should be applied as has been used for other birth defects, including joint planning and communication between medical and social services on the one hand and school systems on the other. Stability of the family environment in which the child is reared is necessary for all children, but is often not available to these children. Furthermore, even when these children are raised in stable foster or adoptive homes, appropriate treatment and schooling are often not available.

It is evident throughout the report that fetal alcohol syndrome tests our ability to provide integrated services that cut across medical disciplines to the mother and child. It also presents major challenges to integrating school and support services for these children. The treatment section of the report emphasizes that, where it is uncertain whether developmental and behavioral characteristics are associated with permanent organic injury, children should be given the benefit of the doubt and have access to treatment measures that may substantially improve their outcome. This has been true, over and over again, for other birth defects, and there is no evidence that suggests it will not prove true for FAS.

I would like to acknowledge the diligence of the committee members and thank them for their efforts. Each contributed in a unique way, bringing both area-specific expertise and a broader perspective to the problem. I enjoyed our challenging discussions. I would also like to thank the IOM staff: Kathleen Stratton for her guidance and coordination of committee activities and her patience at seeing this activity through, Constance Pechura for her perspective and help in putting our ideas into words, Dorothy Majewski for arranging our meetings and transcribing our scribbled edits, and Cynthia Howe for doing whatever needed to be done and her attention to detail.

Frederick C. Battaglia, M.D.
Chair
Committee to Study Fetal Alcohol Syndrome

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We have endeavored to recognize the contributions of all who have assisted the committee throughout the course of this project and any omissions were not intentional.

Report Summary

Fetal Alcohol Syndrome:
Research Base for Diagnosis, Epidemiology, Prevention, and Treatment

BACKGROUND

It sounds simple: women who drink excessively while pregnant are at high risk for giving birth to children with birth defects. Therefore, to prevent these defects, women should stop drinking alcohol during all phases of pregnancy. Alternatively, women who drink alcohol should not become pregnant unless and until they can control their drinking. More than 20 years ago, when fetal alcohol syndrome (FAS) was first described in the published medical literature, there were high hopes for its prevention. In fact, this-has not been simple, and the biomedical and public health communities are still struggling to eliminate a birth defect that should be absolutely preventable.

Although references to the effects of prenatal exposure to alcohol can be found in classical and biblical literature, fetal alcohol syndrome was first described in the medical literature in France by Lemoine et al. in 1968. Researchers in the United States soon also published a landmark report describing a constellation of birth defects in children born to alcoholic women (Jones and Smith, 1973). FAS has since been described in most countries of the world. Briefly, FAS refers to a constellation of physical abnormalities, most obvious in the features of the face (see Figure l-l) and in the reduced size of the newborn, and problems of behavior and cognition. These latter features lead to the most concern. FAS does not refer to signs of acute alcohol exposure or withdrawal at birth. Newborns can have blood alcohol levels high enough to affect acutely their central nervous system function and not have FAS. Newborns can also have no alcohol in their bloodstream *af rhe time of delivery* but still have FAS. An FAS baby is not a "drunk" baby.

The degree of abnormality in any one measure can vary greatly between individuals and can change with time in the same individual. For example, people diagnosed with FAS can have IQ scores from well within the normal range to the severely mentally retarded range. The physical anomalies can be slight or quite striking. Some people with FAS live fairly normal lives if given adequate and structured support throughout their lives, whereas others are severely impaired. The defects may or may not be apparent or easily diagnosed at birth. Although the manifestations of the damage might change with age, FAS never completely disappears, and as with many developmental disabilities there is no cure, although there might be some amelioration in some individuals.

The costs of FAS and related conditions can be quite high--for the individual, for the family, and for society. Three groups have tried to estimate these costs, and these estimates vary greatly (Bloss, 1994). These figures are offered not as established facts but they are intended to emphasize that regardless of the details, or any one specific estimate, the costs of FAS to the individual and society are high. The estimates are problematic because of uncertainties regarding the incidence and prevalence of FAS and uncertainties related to the full extent of health (and other) problems
experienced throughout the lifetime of people with FAS. Incidence rates in several of the most complete studies are similar--on the order of 0.5 to 3 cases per 1,000 births. There is a lack of longitudinal data on the extent of possible problems of adults with FAS. Therefore, annual cost estimates for the United States range from $75 million (Abel and Sokol, 1991) to $9.7 billion (Harwood and Napolitano, 1985).

Since publication of the papers by Lemoine and by Jones and Smith, the biomedical, public health, research, and public policy communities have devoted much time and energy to a fascinating problem of teratology (the study of the effects of chemical exposure on the developing fetus), neurobiology, disease prevention, and social disarray. The U.S. Public Health Service has spent millions of dollars in research, public education, and service programs related to the topic. Important concepts have been established through research. For example, well-controlled research on rats, mice, and nonhuman primates has **demonstrated that alcohol exposure causes** FAS **despite early questions about other causes. However, while**

alcohol is the necessary teratogen, it alone may not be sufficient to produce FAS either in animals or in humans. As with most teratogens, not every fetus exposed to significant amounts of alcohol is affected. The outcomes might be modulated by numerous biologic and environmental factors, such as nutrition, threshold, timing, genetic susceptibility, pattern of alcohol exposure, or fetal resilience. Further research is needed to fully elucidate the factors that influence the expression of alcohol teratogenesis.

Public education campaigns have taught many women and their partners, as well as the medical community and society at large, that excessive alcohol consumption is dangerous during pregnancy. Reduction in the occurrence of substance abuse during pregnancy, reduction in the incidence of FAS, and an increase in the questioning of patients by health care providers about alcohol and other drug use are among the goals of the Public Health Service's Healthy People 2000 initiative (U.S. Department of Health and Human Services, 1991). See Table l-l.

The emergence of crack cocaine as a major public health problem in the 1980s led to worries about a generation of crack babies who would cost the medical care system, primarily neonatal intensive care wards, huge amounts of money and who would overburden the education and social service systems with problems attributable to prenatal exposure to cocaine. Further research has shown that although crack cocaine can lead to serious obstetrical complications and that some of the exposed newborns do have problems. Cocaine-exposed children have not been followed as extensively or for as long a time as alcohol-exposed children; what data have been published show some effects of prenatal cocaine exposure at three years of age, but the problems do not seem to be nearly as devastating as predicted, nor as severe as the long-term problems associated with alcohol exposure. In fact, some of the long-term effects associated with prenatal cocaine exposure may be due primarily to the concurrent use of alcohol during pregnancy.

At the time, however, the cocaine epidemic and its potential risks to unborn children led to heated public policy debates. Policies of mandatory urine testing in delivery wards, and subsequent removal of a child from the care of a mother who tested positive for illegal substances, were instituted in many places (Blume, in press). The unintended negative consequences of these actions have led to a reconsideration and reversal of these policies more recently. The federal government invested millions of dollars in demonstration projects for services for substance-abusing women. Some of these programs included prenatal alcohol exposure, but the emphasis was usually on drugs, particularly illegal ones, other than alcohol, or on polydrug use.

FAS is a complicated health and social problem and, for this reason, potentially involves many different sectors of the government. The U.S. Public Health Service (USPHS) contains the agencies with primary responsibility for research in the area. The National Institute on Alcohol Abuse and Alcoholism (NIAAA) of the National Institutes of Health (NIH) has the lead role in research on FAS. However, NIAAA is a relatively small institute of NIH; their budget is therefore limited. NIAAA programs related to FAS include basic animal research, which has been the mainstay of research in this area; clinical and epidemiologic research on the effects of low to moderate alcohol use by pregnant women; and prevention research. In addition, many research programs sponsored by NIAAA have ancillary importance to FAS, for example, the research it funds on the epidemiology of drinking by women or on general approaches to the prevention and treatment of alcohol misuse.

Another key USPHS agency involved in FAS work is the Centers for Disease Control and Prevention (CDC). CDC's role is to collect data to define the scope of the problem; support the development and evaluation of FAS prevention projects; and build state capacity for coordinated, state-based FAS surveillance and prevention programs (CDC submission to IOM committee). As with NIAAA, CDC has ancillary programs related to maternal and child health, alcohol misuse, and epidemiologic surveillance that can support and inform FAS programs.

Other agencies in the USPHS maintain important programs related to FAS, but these programs have much less emphasis on research. The Indian Health Service, the Health Resources and Services

Administration (HRSA), and the Substance Abuse and Mental Health Services Administration (SAMHSA) fund services or demonstration projects directly or indirectly related to FAS. At this time, no agency has been able to support research on the clinical aspects of FAS, on the medical treatment of children with FAS, or on the education and remediation of these children.

THE CHARGE TO THE COMMITTEE

In recognition of the seriousness of this problem, the U.S. Congress mandated in Section 705 of Public Law 102-321, the ADAMHA Reorganization Act, that the Institute of Medicine (IOM) of the National Academy of Sciences conduct a study of FAS and related birth defects. The National Institute on Alcohol Abuse and Alcoholism on the National Institutes of Health funded the project. This report is in response to that mandate.

The Committee to Study Fetal Alcohol Syndrome was convened in mid-1994. Committee expertise included pediatrics, developmental psychology and neurology, obstetrics, nosology, teratology, epidemiology, substance abuse prevention and treatment, and psychiatry. The charge to the committee was to improve the understanding of available research knowledge and experience on:

- tools and approaches for diagnosing FAS and related disorders,
- the prevalence of FAS and related disorders in the general population of the United States,
- the effectiveness of surveillance systems, and
- the availability and effectiveness of prevention and treatment programs for these conditions.

As part of its work, the committee reviewed U.S. Department of Health and Human Services agency plans to conduct research on the topic and provided guidance for the future.

The committee understood its charge to focus on the effects of exposure to large amounts of alcohol, that is, on FAS and what had historically been called fetal alcohol effects (FAE). The committee studied data on the relation between low or moderate levels of prenatal alcohol exposure and more subtle psychologic, educational, developmental, and behavioral abnormalities associated with such exposure, but given the currently available data it was unable to conclude that these subtle abnormalities do or do not represent a distinct clinical entity. Thus, the committee concluded that it was inappropriate to develop diagnostic criteria or establish incidence or prevalence estimates for this putative condition. However, some discussion of these data is warranted.

Large prospective studies conducted in several U.S. cities have found statistical associations between low to moderate levels of prenatal alcohol exposure (levels not documented or believed to cause FAS) and effects on a variety of behavioral, educational, and psychological tests. These statistical associations are typically weak and the estimated average effects are usually small, so these results seem to have little clinical significance for individual children. The population implications, in theory, can be important for the following reasons. First, one interpretation of these results is that the *small shift in the average* behavioral, educational, and psychological scores in children prenatally exposed to low levels of alcohol theoretically may translate into increases in the number of children below low performance thresholds and decreases in the number of children above high thresholds. Second, these weak population results could also suggest that prenatal exposure to low levels of alcohol occasionally but only rarefy lead to behavioral, educational, and psychological effects in an individual that do have clinical significance. The clinical significance of small population effects on an individual has not been demonstrated empirically for low-level prenatal alcohol exposure. Finally, these population effects suggest at least a teratologic potential for low-level prenatal alcohol exposure and can provide directions for further research. Alternatively, it is possible

that these effects are spurious, given the difficulties of excluding confounding variables such as stress or nutrition by history alone. Given the current state of our knowledge, it is impossible to conclude whether or not low-level alcohol intake in pregnancy has deleterious effects of clinical significance.

The committee is cognizant of the grave concern of many pregnant or preconceptional women and their partners about possible effects of less than heavy consumption of alcohol, and it is also aware that this issue has been and will continue to be debated in the lay press. The committee hopes its report will clarify research questions and design issues for further work in this area. The Jack of diagnostic criteria for or more definitive statements regarding possible effects of low to moderate exposure to alcohol should not be interpreted as contradictory to the Surgeon General's warning against drinking alcohol during pregnancy, which the committee agrees is sound public health advice.

The committee did not establish precise lower limits of alcohol exposure associated with significantly increased risk of FAS. Some researchers have attempted such calculations, but the committee felt that it is premature to make such a statement. Maternal factors such as parity, age, history of heavy drinking, and general health status all influence how much alcohol exposure is necessary for FAS. The level of alcohol exposure is generally very high and likely found in only a small percentage of women who drink while pregnant. Recent data suggest that although approximately 40 percent of all women in the United States are abstinent (Wilsnack et al., 1994), approximately 14 percent of women drink more than 6 drinks when they drink (Witsnack et al., 1994) and approximately 4 percent of women have alcohol abuse or alcohol dependence problems (Grant et al., 1994).

Alcohol abuse and alcohol dependence have fairly specific meaning in the fourth edition of the Diagnostic and Statistical Manual (DSM-IV). However, these terms are frequently used as umhrclla terms for maladaptive patterns of alcohol use. In this report on FXS, the committee has chosen to use alcohol abuse in this general way to indicate heavy drinking, including binge-drinking, that is risky for the given individual circumstances. If a strict DSM-IV diagnosis is intended, it will be so noted. Similar conventions will be used for substance abuse, which is treated very similarly in DSM-IV (American Psychiatric Association, 1994). It should be noted that there are no specific levels of consumption associated with alcohol abuse, either as used in DSM-IV or as an umbrella term in this report. Survey data from 1992 show that approximately 4 percent of all women and approximately 4 percent of women between the ages of 30 and 44 years of age could be considered to satisfy the DSM-IV criteria for alcohol abuse and alcohol dependence (Grant et al., 1994).

FETAL DRUG EFFECTS

Alcohol is one of a number of chemically diverse compounds currently recognized to be toxic to the developing central nervous system (CNS) of humans. Tie neurotoxic properties of these compounds have generally been confirmed in animal studies. Based on their effects, these agents can be divided into two classes of neurotoxicants: some are teratogens in that they produce CNS malformations with associated neurobehavioral dysfunction (e.g., alcohol, methylmercury), whereas others produce neurobehavioral dysfunction in the absence of CNS malformations (e.g., lead, polychlorinated biphenyls). **Alcohol** is a recognized human teratogen that produces fetal alcohol syndrome (FAS) and a variety of other alcohol-related effects in children exposed during prenatal life. Of all the substances of abuse, including heroin, cocaine, and marijuana, alcohol produces by far the most serious neurobehavioral effects in the fetus.

It is convenient to divide prenatal development into three periods: the predifferentiation period, the period of the embryo, and the period of the fetus. The distinction, however, is only conceptual. The conceptus, throughout gestation, is in a continual state of orderly biochemical and structural transition during which new constituents are being formed and spatially rearranged. At any time in the total span of development, these ongoing processes can be subtly deflected, severely perturbed, or abruptly halted, resulting in death or abnormal development. Furthermore, although the effects of exposure during specific stages or "critical periods" of development are probably best documented for the anatomical or dysmorphogenic effects of various teratogenic agents, data on stage-specific effects on growth and functional deficits are increasing, particularly in reiation to prenatal alcohol exposure.

The teratogenic effects of prenatal alcohol exposure can be influenced by numerous factors, both biological and environmental. The complex nature of these multifactorial influences is illustrated in Figure 2-2. This figure attempts to illustrate the point that the expression of adverse alcohol effects in the offspring from birth to adulthood can be influenced by factors that include the critical period during pregnancy when exposure occurs, the pattern and amount of maternal alcohol intake, and a host of biological and environmental variables that can impact both the pre- and the postnatal periods.

The human experience with exposure to alcohol in pregnancy corroborates some of the central developmental concepts in the animal research. These concepts include diversity in the degree of injury to fetuses with comparable alcohol exposure, the potential for injury throughout fetal life, a relationship between level of alcohol exposure and degree of injury, and the importance of both biological variables and the postnatal environment in influencing outcome.

DIAGNOSIS AND CLINICAL EVALUATION OF FETAL ALCOHOL SYNDROME

A medical diagnosis serves several major purposes: to facilitate communication among clinicians; to facilitate communication between clinician and patient (including, in this instance, the parents of patients); to assist in the study of pathophysiology and etiology; and to guide treatment. Two requirements are typically used to evaluate diagnostic criteria. First, the criteria must be reliable. Second, they must be as valid as possible.

The concept of reliability refers to agreement among clinicians and consistency over time. Validity refers to the relevance or clinical utility of a set of diagnostic criteria. Theoretically, criteria can be highly reliable and yet totally invalid. If nosologists were to decide, for example, that height should be used as a criterion for diagnosing mental retardation, since it can be measured in a reliable manner, they would be choosing a criterion that had excellent reliability but no validity. Clearly, therefore, it is important that diagnostic criteria contain components that are clinically meaningful and that lead to correct inferences about the nature of the pathological process.

A number of practical considerations also inform decisions about diagnostic criteria. While reliability and validity set important standards that should be achieved in a good diagnostic system, the day-to-day process of deciding which specific signs and symptoms or other diagnostic indicators should be applied may depend on the clinical context in which a set of criteria is likely to be used. In the everyday world, diagnostic criteria are used for a variety of purposes.

Placing a patient in a diagnostic category confers both benefits and disabilities. The diagnosis of FAS may validate a patient's disability and facilitate appropriate interventions and social benefits. On the other hand, the diagnosis may also be used to stigmatize and to create self-fulfilling prophecies about the future that could be detrimental to the patient and his or her family. Therefore, when diagnostic criteria are developed, nosologists must be sensitive to the various purposes for which these criteria will be used.

A descriptive function is a second important practical purpose of diagnostic criteria. Once criteria for an illness are defined, they are typically used to teach clinicians .how to make that diagnosis. The increasing interest in making diagnoses more objective and reliable has led to the widespread use of diagnostic criteria in a variety of settings: by epidemiologists, third-party payers, forensic experts, and educators, as well as the clinicians for whom they were originally developed. The items selected for inclusion in the criteria are typically assumed by these various "consumers" to be the definitive description of the disorder. If signs or symptoms are not included in the criteria, they are often considered unimportant.

A final issue that arises in deciding on the explicit items to be used in diagnostic criteria is whether the conceptual construct should be narrow or broad. This issue is clearly related to both the gatekeeping function and the descriptive function. Decisions that are made within the context of this issue can have far-reaching implications. One solution to resolving the "narrow versus broad" issue is to create two sets of criteria, one to be used for research and the other for clinical applications. If this is done, then the research criteria are typically more narrow, while the clinical criteria are more broad.

The key issues noted by the committee for identification of FAS include the following:

1. Should a documented history of exposure to alcohol be required for the diagnosis of FAS?
2. Which physical features should be used to define the disorder?
3. Can behavioral or cognitive features be used to define the disorder?
4. Is there a role for ancillary measures (e.g., magnetic resonance imaging [MRI]) in making the diagnosis?
5. Can criteria be designed to be used across the life span?
6. What is the relationship of so-called fetal alcohol effects to fetal alcohol syndrome?

One of the key charges to the committee was to review and evaluate the diagnostic criteria for FAS and related conditions. The committee studied the previous diagnostic criteria and felt that some of the issues confusing the clinical and research communities could be resolved with fairly minor changes in the diagnostic categories and criteria. These new criteria can be found in Table 4-1.

The diagnostic criteria for FAS as described in the preceding section are found under category 1, FAS with confirmed maternal alcohol exposures. A diagnosis is placed in this category when anomalies are found in face, brain, and growth, and a clear history of alcohol exposure is obtained. The committee defined relevant prenatal alcohol exposure as a pattern of excessive intake characterized by substantial, regular intake or heavy episodic drinking. Evidence of this pattern may include frequent episodes of intoxication, development of tolerance or withdrawal, social problems related to drinking, legal problems related to drinking, engaging in physically hazardous behavior while drinking, or alcohol-related medical problems such as hepatic disease. It is anticipated that patients in this category would remain the template for further delineation of the condition.

Category 2, FAS without confirmed maternal alcohol exposure, in Table 4-l is assigned to patients with all the clear phenotypic features necessary for an FAS diagnosis but without a confirmed history of alcohol exposure. Many patients -with FAS are in foster or adoptive placements and their prenatal exposure histories are unavailable. In other cases, the birth mother honestly cannot recall the specifics of her alcohol use in gestation or remains in denial of her alcohol abuse. It is unfair to deny these patients the clinical benefits of a medical diagnosis, but it also seems imprudent to combine their cases with those in category 1 when carrying out some forms of research. Therefore, it is recommended that they be grouped separately.

It also remains theoretically possible that individuals might be found with the full FAS phenotype and a confirmed negative history of gestational alcohol exposure. (Phenocopies do exist for nearly every condition.) Although we are not aware that this situation has arisen yet, such cases should not be considered in category 2. They do not have FAS.

Category 3, partial FAS with confirmed maternal alcohol exposure, is assigned to patients with a confirmed exposure to substantial amounts of alcohol in gestation, some components of the facial features of FAS, and any of the following: evidence of growth deficiency, CNS neurodevelopmental abnormalities, or a complex pattern of behavioral and cognitive abnormalities. This diagnostic category allows an FAS diagnosis to be given to someone who would not receive a Category 1 diagnosis, FAS with confirmed maternal alcohol exposure. This diagnosis could be particularly useful, for example, for some patients who present for diagnosis as an adult. The natural history of FAS is such that some of the "hallmark" indicators used in infancy or childhood are not maintained into adolescence or adulthood. For example, facial dysmorphia can become less distinct. Absent good medical records of dysmorphia or growth retardation at birth and early infancy, an FAS diagnosis otherwise could not be given without Category 3. This diagnosis would also be given to those young children whose growth metrics are within normal ranges, which some studies suggest can occur if the mother cuts down her alcohol exposure in the third trimester. This diagnosis can also be used as a "holding" category as a means to defer a diagnosis of Category 1, FAS with confirmed maternal history of alcohol exposure, until more data collection or evaluation, including documentation as to whether behavioral and cognitive abnormalities persist over time, can support a more definitive diagnosis. In the newborn, for example, there is some controversy whether some behavioral abnormalities, such as abnormalities of state regulation, indicate or predict long-term dysfunction due to fetal alcohol exposure. In such cases, documentation of abnormalities over time would be important.

The naming of this diagnostic category was challenging for the committee, who found no perfect solution. The committee intends for this diagnostic category to include people with signs and symptoms attributable to significant prenatal alcohol exposure and who need medical, social services, and other attention. "Partial" denotes, to some people, that the condition might not be as severe, which the committee did not wish to imply. The committee settled on the use of "partial" despite these reservations. This category, and its name, should remain flexible. As further research reveals the range of the manifestations of FAS, this diagnosis should evolve to be consonant with new data. This diagnosis can be used to categorize such patients for future use in studying and understanding the condition.

The term fetal alcohol effects (FAE) was initially proposed (Clarren and Smith, 1978) as a term for use when an adverse birth outcome could be proven to be related to alcohol exposure in utero. Generally, this term is properly used in animal models of alcohol teratogenesis and in large prospective group studies of humans exposed to alcohol prenatally. The term was not meant for use with individual patients. Terms such as "suspected fetal alcohol effect" and "possible fetal alcohol effect" were suggested as entries on differential diagnostic lists, but this approach has not been well understood. Later, the term alcohol-related birth defects, was suggested for clinical use with this category of patient (Sokol and Clarren, 1989). This term presents clinical problems because most patients who seek diagnosis and do not have FAS, but were alcohol-exposed, do not have major malformations of organs; rather, they have evidence of CNS neurodevelopmental abnormality. The term "birth defects" generally is understood by most lay people to refer to gross structural anomalies, although the March of Dimes defines birth defects as abnormalities of either structure or function.

The committee believes that it may be helpful to subdivide this patient group of ***possible*** prenatal ***alcohol-related*** *effects* into two groups listed in the Table 4-1 as categories 4 and 5. Category 4 is reserved for patients with physical anomalies "alcohol-related birth defects" (ARBD), and category 5, "alcohol-related neurodevelopmental disorder" (ARND), is reserved for patients with neurodevelopmental problems. These diagnostic categories include clinical conditions for which clinical or animal research has linked maternal alcohol ingestion to an observed outcome. A history of confirmed maternal alcohol exposure is required for these diagnoses. The relevant history remains as defined for FAS, but the committee notes that as further research is completed and as, or if, lower quantities or variable patterns of alcohol use are associated with ARBD or ARND, these patterns of alcohol use should be incorporated into the diagnostic

criteria. Whereas patients in categories 1, 2 and, 3 are mutually exclusive, patients could be in both categories 4 and 5. Individuals in categories 4 and 5 must have documented history of prenatal alcohol exposure as described for FAS. Because of the variability in the specific presentation of FAS, ARBD, or ARND, these diagnoses are most valuable clinically if accompanied by a description of the specific problems experienced at the time by the patient. Only with such data will FAS, ARBD, and ARND, be better understood .

Conclusions and Recommendations

The committee-revised diagnostic criteria aim to increase clarity, rigor, and consistency by expanding the traditional designations of fetal alcohol syndrome and other possible alcohol-related effects. The key recommendations inherent in this new diagnostic scheme include the following:

- preserving the criteria for FAS diagnosis but now specifying whether or not prenatal alcohol exposure is documented;
- subdividing the diagnosis of other alcohol-related effects to distinguish physical anomalies from neurobehavioral and cognitive deficits, which can occur separately; and
- adoption and use of the revised criteria for classification and diagnosis by clinical and research professionals in the field.

Research recommendations include

- research to evaluate the utility, reliability, and validity of this scheme for classification and diagnosis;
- research, both cross-sectional and longitudinal, to assess the characteristics and clinical expression of these syndromes across the life span, particularly after adolescence;
- investigation of the differences in expression and specificity of behavioral and cognitive deficits in FAS and ARND;
- research to identify potential structural or functional brain abnormalities and other neurobiological indices that may be associated with, or distinguish, FAS, ARBD, or ARND, and to relate these abnormalities and indices to cognitive and behavioral correlates;
- further clinical research, as well as research using animal models, to examine the adverse developmental effects of prenatal alcohol exposure, and to develop more specific biologic markers for diagnosis (e.g., biomarkers to confirm maternal alcohol exposure; endocrine signals, imaging techniques); and
- consideration of the potential role of fetal alcohol exposure, as appropriate, in developmental disability studies in general.

SURVEILLANCE AND EPIDEMIOLOGY OF FAS

The literature on the epidemiology of FAS and ARBD or ARND is extensive and complicated by differences in the definition of outcomes in this evolving field. Although prospectively gathered FAS incidence rates have been published in more than 20 different studies (see Abel and Sokol, 1987, 1991; Abel, in press), many of the estimates from the United States are based on high-risk populations living in

lower-socioeconomic urban areas. Studies that have produced rates, or estimated rates, of the incidence of FAS have been carried out in a number of countries (see Table 5-1). The literature is far from consistent or conclusive. Various studies reporting the occurrence of FAS range from 0.6 to 3 births per 1,000 in most populations, with some communities having much higher rates. A limited proportion of mothers who are very heavy drinkers will have children with FAS (Abel, in press); several studies have shown that within some communities a small number of women give birth to most of the children with FAS. It is vital that researchers do more to study and compare the social and biological characteristics of FAS mothers with those especially heavy drinkers who do not have FAS children.

Population-based studies can assist in addressing some of the criticisms mentioned above and may be useful for comprehensive prevention efforts. The four major population-based studies done in the world to date were all carried out almost exclusively in Native American communities in North America. In these population-based studies, active and extensive community outreach is carried out for case finding, and all children in a particular population are screened for any physical features (e.g., dysmorphology or low birth weight), family history, or other background characteristics that might make them candidates for the diagnosis of FAS or ARBD.

The overall significance of these population-based studies is that they may provide more accurate prevalence data and could point the way to more valuable information for comprehensive prevention programs. By not looking only at the prevalence and characteristics of FAS, ARBD, and ARND as presented in various clinics, population-based studies possess the capability of examining a range of social and cultural influences impact upon the rate of these conditions. Such conditions may be readily amenable to the design of large-scale or intensive preventive efforts. For example, the rate of maternal risk and the characteristics of the social milieu could help define adequate approaches and targets for prevention and the magnitude of effort required.

On a national level, there are two ways to monitor the impact on public health of alcohol use during pregnancy by using surveillance or epidemiologic strategies. The two surveillance approaches discussed in this section involve passive and active methodologies. The advantages and disadvantages of each approach are presented here, along with possible solutions to the problems they pose with respect to FAS. Given the stated goal of reducing FAS, much more attention has to be paid to standardization of data collection, whatever the strategy for assessment.

Passive Surveillance

Passive surveillance is the strategy generally used to monitor birth defects. This strategy simply tallies the number of cases of a defined birth defect or syndrome noted on existing documents, such as medical records, and relates that figure to some population. This is the strategy behind the CDC's Birth Defects Monitoring Program, which used hospital discharge data on both live and stillborn newborns to estimate the incidence of FAS at 2 cases per 10,000 between 1979 and 1992, and 3.7 per 10,000 births in 1992 (CDC, 1993a).

Advantages and Disadvantages

The advantage of passive surveillance for FAS is that it is directly comparable with the methodologies used to assess the incidence of other birth defects, allowing a comparison of relative rates. It allows monitoring of secular changes and differences by geographic distribution or sociodemographic status, as well as comparison of the distributions of different kinds of birth defects.

There are several disadvantages to this methodology, however, for the surveillance of FAS. A major problem is the accuracy with which FAS is diagnosed, particularly at birth. This inaccuracy is due to several factors: (1) it is difficult to evaluate central nervous system (CNS) status at birth; (2) many clinicians are not trained to identify FAS; (3) inconsistent criteria are used for case definition; and (4) clinicians may be reluctant to identify alcohol problems or to label women as having alcohol problems.

Clinicians continue to use, somewhat idiosyncratically, a diverse pattern of traits to diagnose FAS (Clarren and Astley, 1994). There may also be "selective" case finding by physicians who look for particular malformations among some minority groups compared with others (Chavez et al., 1988). In addition, the characteristics that are prominent in FAS and used for diagnosis may differ by age. A survey reported by Clarren and Astley (1994) demonstrated that while clinicians consider microcephaly and growth retardation *to* be important parameters in newborns and infants, in older children they are *more* likely to consider microcephaly in conjunction with behavioral problems as pathognomonic. A solution would be to use the standardized criteria for diagnosis presented in Chapter 4 of this report.

Possible Solutions

Passive surveillance as used currently can be improved for FAS surveillance. Improvements could be made directly by improving passive surveillance of FAS or indirectly by using proxy indicators of FAS. Clinicians can be educated to better recognize FAS. However, it is still likely that biased reporting will continue to occur, given the negative labeling associated with alcohol involvement. It may be difficult to determine accurately the incidence of FAS at birth, particularly in environments where clinicians are not well trained, not sensitive to or willing to report the use of alcohol among pregnant women, or not willing to use standardized diagnostic criteria. Providing a confidential reporting mechanism, separate from the medical record or birth certificate, would reduce this bias. Even in the presence of these improvements, however, correct ascertainment of the rate of FAS at birth remains problematic due to the difficulty in assessing CNS or neurobehavioral abnormalities at this age.

An alternative to monitoring the incidence of FAS at birth is to develop surveillance criteria that would identify a group of newborns with a high probability of having FAS, for example, newborns with birth weights below 2 standard deviations for gestational age. Criteria such as birth weight that are routinely recognized, measured, and noted in the medical record are not subject to clinical judgment. This strategy was adopted in a study of four American Indian communities where the investigators selected a group of children who had a birth weight of less than 3,000 grams. These children were referred for evaluation for FAS if they had poor performance on a developmental screening test or if they had a head circumference below the 10th percentile; 4 out of 24 suspected cases were confirmed as FAS (Duimstra et al., 1993).

Data from the Maternal Health Practices and Child Development Project, an ongoing assessment of the long-term effects of substance use during pregnancy were analyzed for indirect indicators of FAS. This study is a prospective epidemiologic study of pregnancy outcomes, and one of few that have followed a cohort from early pregnancy up to the child's tenth year. The women selected for this study represent the entire spectrum of alcohol use, although the majority were moderate drinkers and moderate users of other substances. The cohort used for analysis was 742 mother-child dyads. Although these data were collected as part of a controlled, prospective epidemiologic study, the data used in the example are representative of data that could be gathered passively for a surveillance effort.

Surveillance criteria for proxy indicators of FAS were defined as either head circumference, weight. or height at birth less than the 10th percentile, and the presence of at least one facial anomaly. The facial anomalies were selected from the list of facial dysmorphic features that are part of FAS.

Children who had a growth deficit at birth, defined as weight or height or head circumference below the 10th percentile, combined with the presence of at least one facial anomaly, were significantly more likely to have been exposed to alcohol prenatally; had significantly lower weight, height, and head circumference at three and six years; and scored significantly lower on the composite score of the Stanford-Binet Intelligence Scale. It was not possible, in this moderately exposed population, to estimate the incidence of FAS, but the strategy may lend itself to such estimates if the sample size is large enough.

To establish a relationship between the incidence of cases with the surveillance criteria and the occurrence of FAS, however, would require replicated investigations using dysmorphologists trained in the identification of FAS and follow-up of these research cohorts over the first few years to determine the predictability of the surveillance criteria to the diagnosis.

The advantages of a surveillance program using indirect measures or indicators lie primarily in three areas: (1) lower cost, because the criteria are already ascertained and noted in the birth record; (2) more accurate measurement of the criteria; and (3) elimination of the problem of negative labeling of women by clinicians.

The disadvantages of this method lie in the general problem of extrapolating from the surveillance criteria to the incidence of FAS and include pervasive problems pertaining to the diagnostic abilities of clinicians, patterns of drinking, and the rates of alcohol use and alcohol abuse within the populations being evaluated. In addition, a decrease in the prevalence of the indirect marker would not necessarily reflect a proportionate decrease in the prevalence of FAS.

In passive surveillance--whether direct or indirect measurement is used--it is important to monitor multiple sources for the detection of cases (e.g., birth and death certificates, Medicaid claims, private pediatric practice case files) because no one source can identify more than a minority of cases (CDC, 1993b).

Active Surveillance for Fetal Alcohol Syndrome

Active surveillance implies direct collection of data using experimentally driven protocols rather than using available data such as medical charts. The hallmark of these kinds of protocols is the prospective epidemiologic study. In this study every case is followed from a predetermined entry point (time A) to a specifically defined end point (time B; e.g., birth). There have been few examples of active surveillance outside the focused research literature. Most of these studies have had small sample sizes; they are far from representative; and the diagnostic criteria are not consistent (see clinic-based studies in Table 5-l). In general, the rates of FAS are higher by an order of magnitude than those estimated from passive surveillance studies (Abel, in press; Abel and Sokol, 1987, 1991; May, in press).

Advantages and Disadvantages

As illustrated above, a comparison of the incidence rates generated by active and passive surveillance demonstrates that active surveillance detects substantially more cases (Klaucke, 1992; May, in press). Moreover, control over data collection also implies control over data quality. Thus, the diagnoses are more likely to be valid and reliable. Because of this, direct and more accurate measurement of the rate of FAS is possible using active surveillance. Population-based active surveillance can be tailored to characteristics of the population under study and can be linked more closely with prevention efforts.

The disadvantages of active surveillance are threefold: (1) it is very expensive to collect data from a population large enough to yield accurate rates; (2) it is extremely labor intensive; and (3) it is selective, in

that only women who appear at time A (entry) will be assessed at time B (birth). One report noted a tenfold difference in costs between active and passive surveillance (Klaucke, 1992). Active surveillance programs are usually centered in large cities and within academic and research facilities. As a result, the data are likely to be biased and cannot be extrapolated to the general population. Few cases of FAS were identified in the major prospective epidemiologic studies of maternal substance abuse in major U.S. cities, e.g., Seattle and Pittsburgh.

Just as passive surveillance can be refined by using or including indirect measures that focus on birth weight for case finding, so too can active surveillance of alcohol abuse be used indirectly to measure or at least approximate the success of prevention efforts. This is because FAS has a known cause--alcohol abuse. Because FAS, by definition, occurs only among offspring of women who abuse alcohol, a logical point for screening would be alcohol abuse. A screen for alcohol abuse would yield a low rate of cases but would identify women who are at high risk of having a baby with FAS, ARBD, or ARND. This type of screening has two advantages: (1) it identifies the population that is at the highest risk of having a child with FAS, and (2) it identifies a population that is unquestionably in need of intervention.

The disadvantages of this approach, however, are numerous: (1) the diagnosis of alcohol abuse is often unreliable, (2) the diagnosis of alcohol abuse is often avoided by clinicians to preclude labeling women, and (3) women may not report symptoms of alcohol abuse. The rate of FAS among the offspring of women who abuse alcohol is not known; the few estimates available are relatively low (Abel, in press; Abel and Sokol, 1987), and the estimates show a varying rate by birth order (Abel, 1988). Thus, prescreening for alcohol abuse to estimate FAS is problematic.

Similar problems can be seen when we consider measuring drinking or heavy drinking during pregnancy, although this is an attractive option, given the opportunities it would present for prevention and intervention. However, measuring drinking or heavy drinking is time intensive and remains an effort that few clinicians are trained or willing to make. Drinking, particularly heavy drinking during pregnancy, is a stigmatized behavior; it is likely to be underreported by women and reported in a biased fashion by clinicians. Moreover, we do not know how "heavy" heavy drinking must be to result in FAS, ARBD, or ARND and we may never be able to arrive at a consensus because of the numerous other social, personal, and biological factors that interact with alcohol consumption to produce FAS, ARBD, and ARND (Abel and Hannigan, in press).

Feasibility of Surveillance

Surveillance of FAS can be accomplished by actively seeking or ascertaining cases of FAS or by establishing surveillance criteria for proxy indicators of FAS and monitoring the incidence of cases that meet those criteria. Some suggestions for doing this have been described above. Given the limitations of passive surveillance for FAS, it is possibly more efficient to monitor or actively ascertain the incidence of cases that meet surveillance criteria and then estimate the rate of FAS. This would require research to validate the criteria, to establish the accuracy of their measurement and reporting, and to determine an appropriate estimation (or "conversion") factor. Population-based surveillance projects in representative regions across the country might be useful for providing this "conversion" factor. Given the inadequacy of passive surveillance for estimating the magnitude nationally of the FAS problem, for indicating success or failure of prevention efforts, and for identifying FAS children and families in need of clinical, social, and educational services, other approaches need to considered, expanded, and validated.

Conclusions and Recommendations

The committee concludes that FAS, ARND, and ARBD are .a completely preventable set of birth defects and nemodevelopmental abnormalities and that FAS is arguably the most common known nongenetic cause of mental retardation. Further, ARND and ARBD are reported to occur *even more* frequently than FAS. Thus, the results of heavy prenatal alcohol exposure constitute a major public health concern. The committee endorses the efforts of the Centers for Disease Control and Prevention to move away from passive surveillance methods, which have been unsuccessful in defining the magnitude of this problem, but recognizes that no national baseline is available to judge the impact of public health and other preventive interventions. The committee encourages CDC's new efforts to implement active surveillance strategies in state- and university-based surveys.

However, to address the lack of baseline data and the wide variation of prevalence estimates, for subpopulations, including ethnic minorities, the committee recommends that

- an interagency plan be developed for a national survey to estimate the prevalence and incidence of FAS, ARND, and ARBD, which could utilize active surveillance techniques (direct or indirect);
- prevalence surveys of FAS, ARND, and ARBD be repeated at periodic intervals;
- data on prevalence of FAS, ARND, and ARBD be integrated with data on the drinking behavior of pregnant women to improve risk assessment for these disorders;
- improved data collection and surveillance be implemented to identify specifically children with FAS, ARND, and ARBD in various social and educational environments (e.g., maternal and child health block grant programs, Head Start programs, and Early Intervention and Special Education Services); and
- when active surveillance strategies are employed that identify children with FAS, ARND, or ARBD, appropriate linkages should be in place among agencies and local clinics to facilitate treatment.

RESEARCH ON WOMEN'S DRINKING AND ON PREGNANT WOMEN'S DRINKING

Publicity about FAS has undoubtedly increased concern about women's drinking and vice versa. However, these two major areas of research have remained relatively isolated from one another. FAS-oriented research on pregnant women who drink has focused primarily on measuring alcohol consumption and on identifying women at risk for giving birth to children with FAS, ARBD, or ARND because of their alcohol abuse. Much of this research, however, has paid relatively little attention to psychological and social determinants of maternal drinking behavior. Although surveillance studies have monitored trends in alcohol consumption among women of childbearing age, such surveys are restricted for the most part to assessing a few demographic characteristics, and most have serious limitations in their measurement of alcohol use, reproductive history, and potential predictors of drinking patterns. Studies of pregnant women have rarely attempted to apply findings from recent research on drinking among women in general to better understand influences on *pregnant* women's drinking behavior.

Although researchers have seen changes in drinking patterns during pregnancy over the years, there is no substantive evidence of any change in drinking behavior among women who drink more heavily or abuse alcohol, either in terms of proportions of heavy drinkers at the time of conception or in terms of consumption levels during pregnancy (Hankin et al., 1993a,b). To learn why some pregnant women continue to drink at hazardous levels despite factual knowledge about fetal risks, it is vital to understand the personal and social-environmental risk factors that support maternal drinking (May, in press; Waterson and Murray-Lyon, 1990; Weiner et al., 1989). Related research on women's drinking more generally may provide some answers for understanding the determinants of pregnant women's drinking behavior.

A shortcoming of current clinic-based studies is that most include relatively small numbers of women who are heavier drinkers, alcohol abusers, or alcohol dependent. Most women drinkers stop or drastically

reduce their drinking when pregnant (Serdula et al., 1991). In one study, for example, only 4.6 percent of women reported drinking an average of one drink per day by the end of the third trimester of pregnancy, compared with 44 percent reporting one or more drinks per day before pregnancy (Day et al., 1993). While this striking reduction in alcohol consumption during pregnancy may reduce fetal risk, the small numbers of heavier drinkers in most clinic-based studies, and the limited variation in drinking levels among pregnant women who do drink, reduce the statistical "power" to detect predictors of maternal drinking behavior.

Another limitation of many clinic-based studies is that most have measured only a few demographic characteristics as predictors of maternal drinking and its effects. Few studies of drinking during pregnancy assess personality or social-environmental variables associated with drinking. Factors such as depression, low self-esteem, family history of alcoholism, partner drinking, sexual dysfunction, and sexual abuse or other violent victimization have related to drinking in studies of women in general (e.g., Miller et al., 1993· Wilsnack, in press, a,b) and may be predictive of drinking behavior for pregnant women as well. Also largely unexplored are the dietary behaviors that may affect biological susceptibilities to alcohol's effects (Abel and Hannigan, in press). Learning more about such personal, social, and biological risk factors for drinking in pregnancy might permit prevention efforts to be targeted more effectively to specific maternal risk drinkers.

One way to overcome the limitations of smaller and less representative clinical samples is to survey large representative samples of pregnant women in the general population. Because only a small percentage of women are pregnant at any point, only general population surveys with very large samples will allow reliable analysis of drinking correlates among women pregnant at the time of the survey. Unfortunately, many of the largest national alcohol and health surveys (some with samples of more than 40,000 respondents) have not included questions about respondents' pregnancy status.

Alcohol consumption patterns among women in the general U.S. population provide a context for discussing drinking behavior of pregnant women. Approximately 60 percent of adult women in the United States. drink alcohol at least occasionally. Of these, the large majority consume small to moderate amounts of alcohol without adverse social, behavioral, or health consequences. Rates of drinking and heavy drinking tend to be highest among young women and to decline steadily with age. Despite concerns about an "epidemic" of alcohol problems in women in the 1970s and 1980s (e.g., Fillmore, 1984), rates of drinking and heavy drinking have been relatively stable among both women and men, with modest increases in the 1970s and modest declines since the early 1980s (Midanik and Clark, 1994; Williams and DeBakey, 1992; Wilsnack et al., 1994).

Available data indicate substantially lower rates of both drinking and heavier drinking among pregnant women, relative to nonpregnant women of childbearing age. For example, less than 25 percent of pregnant women reported any use of alcohol in the 1989 National Longitudinal Survey of Youth (20 percent); the 1988 National Maternal and Infant Health Survey (NMIHS; 21 percent); the 1991 CDC Behavioral Risk Factors Surveillance Survey (BRFSS; 14 percent); and the 1994 National Institute on Drug Abuse (NIDA) Pregnancy and Health Survey (19 percent). By comparison, the NIDA survey estimates that 20 percent of pregnant woman smcked, 5.5 percent used any illicit drugs, 0.9 percent used crack cocaine, and 10 percent used psychotherapeutics for medically-indicated conditions. Trend data suggest a significant decline in prenatal alcohol use during the past decade. For example, annual BRFSS surveys conducted in 21 states between 1985 and 1988 found that pregnant women's self-reports of any alcohol consumption in the past month declined from 32 percent to 20 percent over the study period (Serdula et al., 1991).

Although definitions of heavy drinking vary across studies, rates tend to be very low regardless of the definition used. For example, data from the 1991 BRFSS survey shows that 2 percent of all women of child-bearing age but only 0.3 percent of pregnant women reported drinking 60 or more drinks during the preceding month and 21 percent of all women of child-bearing age but only 1.3 percent of pregnant women

reported **binge** drinking (five or more drinks on at least one occasion) during the preceding month (Centers for Disease Control and Prevention, 1994). Although 45 percent of the respondents to the 1988 NMIHS survey reported drinking alcohol during the 3 months before they learned of their pregnancy, 21 percent drank after they learned of their pregnancy, 0.6 percent had six or more drinks per week during pregnancy, and 0.2 percent reported average consumption of two or more drinks per day (Centers for Disease Control, 1995). In four states collaborating in a Pregnancy Risk Assessment Monitoring System (PRAMS) in 1988-1989, proportions of pregnant women reporting consumption of 14 or more drinks per week ranged from 0.03 percent to 0.13 percent (Bruce et al., 1993). Although these percentages are small in ***relative*** terms, the large ***absolute numbers*** of women who continue to engage in heavy and hazardous drinking throughout pregnancy make it imperative to understand the personal and social factors that make women more likely to continue drinking heavily during pregnancy.

Correlates of drinking in early pregnancy are similar to those for women of childbearing age in general. This is because women often don't know they are pregnant until a month or two has passed. They therefore engage in their customary drinking habits early in pregnancy. The correlates include being Caucasian, older, and more educated (Streissguth et al., 1991). Although a number of studies compare correlates of drinking behavior in earlier versus later stages of pregnancy, little attention has been given to correlates of first-trimester drinking before and after pregnancy is confirmed: Do women who change their drinking patterns immediately upon learning of, or suspecting, pregnancy differ from women who change their drinking behavior more gradually?

Older pregnant women in some national samples were more likely than younger pregnant women to report drinking (Centers for Disease Control and Prevention, 1995; National Institute on Drug Abuse, 1994; Serdula et al., 1991), but the percentage of women over 25 years of age who drank during pregnancy has decreased between 1985 and 1988 to that of women 18 to 24 years of age. The NMIHS, a survey of women who gave birth in 1988, suggests that women who drink while pregnant are more likely to be white, more educated, of a higher income level, married, or smokers (Centers for Disease Control and Prevention, 1995). That same survey showed that heavy drinking while pregnant was more prevalent among women who were more than 35 years of age, non-white, and unmarried. Other factors associated with heavy drinking in these pregnant women were low annual household income and no prenatal care. Other studies tend to support that general profile of pregnant women who drink (Day et al., 1993; Waterson and Murray-Lyon, 1990). Correlates of continued drinking during pregnancy despite information on the risks and referral for intervention include onset of drinking behaviors at a young age, heavy drinking on the part of parents and siblings (especially female relatives), evidence of alcohol-related physical problems, and qualifying for a diagnosis of alcohol dependence (Smith et al., 1987)

Conclusions and Recommendations

The committee concludes that clinic-based studies of pregnant women have included only a limited range of biologic and psychosocial variables as possible risk factors for drinking in pregnancy. Furthermore, most large national health surveys contain inadequate data on women's drinking or pregnancy status. The lack of such data severely limits the ability to predict which women are most likely to engage in high-risk drinking during pregnancy or to give birth to a child with FAS, ARND, or ARBD. Therefore, the committee recommends special attention to the following research questions and issues:

- expand studies of pregnant women, where possible, to include measurement of psychological, social-environmental, dietary, and other factors that may influence women's drinking behavior or fetal outcome;

- inclusion of questions regarding alcohol consumption and pregnancy status in appropriate future national health surveys;
- standardization of questions added to health surveys regarding the quantity, frequency, and variability of alcohol consumption so as to permit comparisons across multiple surveys;
- studies focused on protective factors that may decrease women's drinking or prevent fetal injury from alcohol consumption;
- studies of women who have successfully stopped heavy or abusive drinking; and
- continued and increased epidemiological study of women's drinking patterns, including efforts to maximize the validity of self-report measures, efforts which should include the use, when possible and appropriate, of a biomarker for alcohol exposure.

PREVENTION

Alcohol is a legal drug consumed by many people, but its abuse carries heavy costs-for the individual and for society-apart from costs associated with FAS. Many people who abuse alcohol do not get the help they need, either because they do not have access to the health care or social services system or because some health care or social services professionals are uncomfortable talking with patients about substance abuse problems.

The prevention of FAS, ARBD, and ARND requires a comprehensive program encompassing a variety of approaches. Because prenatal alcohol exposure most likely is associated with a spectrum of effects ranging from negligible to severe, a number of different drinking patterns with various characteristics and etiologies need to be addressed.

The committee found it helpful to think about and analyze the prevention of FAS and related problems within a conceptual framework. Two structures were considered by the committee-the classic framework of primary, secondary, and tertiary prevention (IOM, 1991) and a framework developed by the IOM Committee on Prevention of Mental Disorders (IOM, 1994). In more classical terms, primary prevention refers to a focus on healthy persons and seeks to avoid the onset of disease processes. Secondary prevention involves early detection and treatment of persons with early or asymptomatic disease, and tertiary prevention concentrates on arresting the progression of a condition and on preventing or limiting additional impairment. The committee decided to use the latter framework (IOM, 1994), which describes a spectrum of seven levels of intervention, as a more appropriate tool, with some adaptation, to discuss prevention of FAS, ARBD, and ARND. The hallmark of this framework is that one enters into the continuum of interventions in a manner proportional to the certainty and severity of the risk involved. That is, the intervention becomes more specific and intensive as the risk is defined less by general population characteristics and more by individual characteristics.

The model adapted by the IOM Committee on Prevention of Mental Disorders (IOM, 1994) was originally described by Gordon (1983, 1987). It includes a broad spectrum of prevention measures (see Figure 7-l). The model also illustrates two related components-treatment and maintenance. Prevention activities vary from population-wide programs to efforts aimed at an individual at high risk. Prevention is divided into three levels (universal, *selective,* and *indicated),* treatment into two (case *identification* and *standard treatment* for known disorders), and maintenance into two *(compliance with long-term treatment* and *aftercare*). The model developed by the IOM in 1994 required slight modifications for applicability to FAS, but the general concepts remain the same (see Figure 7-l). The committee to study fetal alcohol syndrome also stresses that core research in fields such as biomedicine, behavioral and social sciences, and epidemiology support, inform, and are vital to research in FAS prevention..

Because significant people in the life of a woman can play a crucial role in encouraging a healthy pregnancy or, unfortunately, encouraging unhealthy practices, the committee took a family-oriented approach to prevention. Clearly, a woman's partner and her community are appropriate targets for preventive interventions and subjects for preventive intervention research. After the birth of an FAS child, there are two targets for intervention-the mother and the child. Each of them is a patient in need of care; each is a target for treatment and maintenance as well as for prevention of problems in future pregnancies.

Universal prevention attempts to promote the health and well-being of all individuals in society or of a particular community. Universal preventive interventions are those targeted to the general public or to an entire population group that has not been identified on the basis of individual risk. Selective preventive interventions are targeted to individuals or a subgroup of the population, whose risk of developing the condition is significantly higher than others by virtue of belonging to that subgroup. There is no assessment of individual risk in selective preventive interventions. Indicated preventive interventions are targeted to someone based on individual risk-factors, not on the basis of belonging to a population. Special considerations related to FAS necessitated some modification of this definition. That is, although preventive interventions are generally thought of as stopping short of treatment interventions, when thinking about a comprehensive prevention program for FAS, ARBD, and ARND, it is clear that ***treatment*** of alcohol problems in women (and their partners) is an appropriate indicated ***preventive*** intervention for the fetus being carried by the woman, as well as for children who might subsequently be conceived and borne by her.

Universal prevention strives to ensure that all members of society understand that drinking alcohol can have hazardous consequences, and it promotes and supports positive, broadly shared attitudes and beliefs to protect the individual from harm due to alcohol consumption. Universal prevention of FAS further strives to ensure that all members of society understand that drinking during pregnancy can have hazardous consequences. One of the basic techniques used in universal prevention is public education. Television advertisements, public service announcements, pamphlets, posters, and the like, which serve to educate the public about the risks of heavy drinking and to encourage responsible drinking are universal preventive interventions that indirectly encourage responsible use of alcohol during pregnancy. Universal prevention could also involve changes to the social environment. Male partners and extended family 'members could play vital roles, as could peer groups (Wilsnack and Beckman, 1984; Wilsnack et al., 1991) and health care providers.

No universally safe level of alcohol consumption has been identified for pregnant women. Current data from many sources suggest that approximately 20 percent of pregnant women drink alcohol at some level during pregnancy (Centers for Disease Control and Prevention, 1995; NIDA, 1994; Serdula, 1991). The vast majority of the babies born to these women show no overt signs of damage. At present, there is uncertainty whether minimal alcohol intake during pregnancy could be associated with any degree of injury to the baby.

Whether or not further research clarifies the putative relation between low to moderate levels of alcohol during pregnancy and adverse birth outcomes, the universal prevention message for FAS is a conservative one that encourages abstinence prior to conception and throughout pregnancy as the safest alternative. This was articulated by the Surgeon General in 1981 (U.S. Public Health Service, 1981). If further research demonstrates a causal relation between 'low or moderate levels of alcohol consumption and less severe or complete manifestations of neurobehavioral damage than seen in FAS, ARBD, or ARND, as has been hypothesized, then this most conservative message of total abstinence will have been wise and reasonable.

An obvious example of a universal preventive intervention specific to FAS is warning labels on alcoholic beverages or similar signs posted in restaurants or bars. There are little data to suggest that these measures have decreased FAS, ARBD, or ARND.

Health care providers can and should engage in universal preventive interventions. Visits to family practitioners and to obstetrician gynecologists offer the opportunity for brief messages about the importance of responsible alcohol use and for providing general information about the risks of alcohol to the fetus. More targeted messages and questioning would depend on whether tke woman drinks and is pregnant.

Universal interventions seem to have increased the general knowledge of FAS and related problems. Many women cut down their consumption of alcohol while pregnant (Serdula et al., 1991). Some pregnant women do not drink simply because the state of pregnancy decreases the palatability of alcohol for them. However, it is likely that increasing awareness of FAS and risks to the fetus have contributed to the decreases. Nevertheless, those same data indicate that women who drink heavily do not cut down their consumption of alcohol while pregnant. It is these women who are at risk for giving birth to an FAS child.

Selective preventive interventions are targeted to people who are at greater risk for a particular outcome because they are members of a subgroup known to be at higher risk than the general population. These interventions involve different levels of targeting and intensity compared to universal preventive interventions. Targets of selective prevention for FAS, ARBD, and ARND include women who drink alcohol and are in the reproductive age range.

The epidemiologic literature related to FAS clearly identifies several risk factors for giving birth to an FAS child. First, and most obviously, is consumption while pregnant of large quantities of alcohol-either continuously or in risky patterns, such as bingeing. For those women who had a baby with FAS and for whom alcohol consumption is known, the levels, pattern, and frequency of alcohol consumed have typically been high.

The partners of women who drink could be included in selective prevention activities as well. In contrast to the attention devoted to the influence of maternal factors on pregnancy outcome, data on the possible role of paternal factors are sparse. The important social, psychological, and behaviorally supportive role that the male partner plays in a healthy pregnancy is well established and cannot be emphasized too strongly. However, the possible biophysiological contribution of paternal alcohol consumption to an adverse pregnancy outcome is not well understood. However, since many women who are at high risk for FAS are unmarried, in very unstable relationships, or both, it is important to tailor interventions to these situations. Contracts with other significant persons or with an entire at-risk community might be useful including extended family, influential peers, and possibly bartenders. Family- and community-wide pledges related to drinking during pregnancy have been used by some Native American communities. These approaches seem to have promise for some communities but have not been evaluated.

Health care providers should be encouraged and educated about the risk factors for FAS and should be trained to appropriately question women about their drinking and contraceptive histories. If a woman drinks alcohol and has other risk factors for FAS, health care providers should deliver selective preventive interventions, and this requires training and preparation.

Several screening tools are available to help identify women who potentially have alcohol abuse problems. Someone who is likely to be an alcohol abuser as indicated by screening should undergo a more thorough assessment of her alcoho! use. Relevant information would include, for example, quantity, frequency, pattern of alcohol use, and level of dependence. (See Illustration 7-5 for an example of a screening tool.) The purpose of screening is to identify health problems or risks in time for intervention to prevent serious consequences such as FAS.

Given the limits of self-reports of alcohol use in many circumstances, an efficient, nonintrusive, valid, and inexpensive biologic marker of alcohol use would be an important tool for accurate screening and diagnosis of women abusing alcohol. Moreover, the availability of biomarkers might lead to earlier. interventions for preventing FAS, serve as an indicator for evaluating FAS prevention outcomes, help

identify instances of maternal under-reporting of alcohol use, and facilitate research on possible dose-response relations between alcohol exposure and adverse health effects, including FAS, ARBD, and ARND.

Although research continues to search for an ideal biomarker of alcohol exposure, no satisfactory laboratory test currently exists. To date, Gamma glutanmyl transferase (GGT), acetaldehyde adducts, and carbohydratedeficient transferrin (CDT) markers lead the way in providing a rather specific and sensitive test for detecting alcohol consumption and/or abuse. A biomarker for alcohol abuse, however, would not be a substitute for a health care provider's verbal assessment of alcohol use by at-risk women. Such interaction can sometimes be the first step in developing a supportive relationship that could be crucial to the woman's progress in achieving abstinence or, at least, moderation.

Counseling about drinking during pregnancy at routine prenatal visits can lead to decreases in alcohol use during pregnancy (Rosen et al., 1981). One particular program was oriented toward positive messages -stressing the increased likelihood of a healthy baby if the woman quit or decreased drinking, and improving the woman's self-esteem. Counselors also made referrals to specialized treatment programs and community agencies. In another project in which counseling and referrals were offered to pregnant women, compared to those who stopped drinking women who drank throughout pregnancy reported having started drinking at a younger age, were more likely to report heavy drinking on the part of their parents and siblings (especially their female relatives), had more evidence of alcohol-related physical problems, and were more likely to qualify for a diagnosis of alcohol dependence.

A pregnant woman who scores positive on a brief screening and has other risk factors should be educated about FAS. This education should be more specific or more involved than that delivered routinely to every pregnant woman. Following a more detailed assessment of risk, interventions should be planned. These interventions will range, as appropriate, from brief interventions to intensive treatment for alcohol dependence. In general, the strength of the intervention should be proportional to the level of risk.

indicated preventive interventions are targeted to high-risk individuals who are identified as having minimal but detectable signs or symptoms foreshadowing a condition or who have biological markers indicating predisposition (IOM, 1994). At present, the only biologic marker to identify an individual woman at high risk for giving birth to an FAS baby is having already given birth to an FAS child (May, in press). There is no prenatal test of fetal damage from alcohol that could be used to indicate a mother who should be aggressively treated to prevent further damage to the child. FAS studies consistently report that women who have had one definite FAS child, and who continue to drink, have progressively more severely affected children with subsequent pregnancies (Abel, 1988; Davis and Lipson, 1984; May et al., 1983).

The committee therefore considers the target for indicated preventive interventions to be a woman who abuses alcohol, including engaging in occasional binge drinking, while pregnant or at risk for being pregnant, particularly a pregnant or preconceptional woman who drinks alcohol and has already given birth to a child with FAS, ARBD, or ARND. As with selective interventions, the committee would also include interventions aimed at the partner, significant friends, or family members of a woman who fits the profile just described. Indicated *prevention* of FAS includes alcohol abuse *treatment* for a pregnant woman or for a woman highly likely to become pregnant. The committee identified little controlled research into the most effective ways to treat pregnant women who drink.

Indicated prevention can be promoted through intensive professional education (Bowen and Sammons, 1988; Davis and Frost, 1984; Little et al., 1981. Because, in many cases, women do not seek obstetric or gynecologic services until delivery, any health care provider who comes in contact with women who abuse alcohol should consider brief intervention therapies and referral to more formal alcohol abuse treatment, if appropriate, and counsel her whether pregnancy is advisable.

The type and intensity of a prevention intervention should be appropriate to the risk involved; thus intensive action should be considered for a woman who has given birth to a diagnosed FAS child. In these cases, because of possible stigmatization of the mother or the child, as discussed in other sections of this

report, diagnoses should be assigned conservatively by qualified dysmorphologists or clinicians skilled in the diagnosis of FAS. However, once a verified case of FAS has been identified, aggressive measures must be taken to reduce the impairment and disability that might axumulate with successive pregnancies and constitute a heavy burden on society and on the woman's health and well-being.

For the comparatively small group of women who continue to abuse alcohol during pregnancy, formal treatment of alcohol dependence may be needed. There are a number of descriptions of comprehensive clinical treatment for pregnant alcohol-dependent women (Finkelstein, 1993; Jessup and Green, 1987; Rosett and Weiner, 1981). The treatment programs described are typically broad, multimodal interventions that are intended to address the complex problems exhibited by this population. Thus, recommended treatmenrs usually encompass medical and obstetric services, as well as alcohol and drug abuse services in the form of individual or group counseling, family therapy, referral to self-help groups, education about alcohol effects, parenting skills training, and case management. As mentioned earlier in this report, however, systematic data collection on characteristics of women who abuse alcohol during pregnancy has been rare. Thus, treatment programs for pregnant alcohol abusers have been based primarily on the availability of services and on clinical judgment, and in the relative absence of empirical data that could inform the conceptualization and development of treatments targeted to address the specific problems of this population.

Equally as important as getting a pregnant women who abuses alcohol to stop drinking is to keep her abuse under control. This is vital to improve her health and well-being as well as to prevent the birth of a child with FAS. The literature in recent years suggest that an effective way to help alcohol-abusing women who had FAS children is through intensive case management (Bacon, 1988; Davis and Frost, 1983; Masis and May, 1991; Rosett and Weiner, 1981; Weiner et al., 1989). Continuation of care into the post-partum period achieves or facilitates many goals. For example, this can eliminate the presence of alcohol in breast milk. It is standard medical advice that women who are breast-feeding not drink, which could further expose the infant to alcohol. Case management of women who have had one or more FAS children can help protect against further FAS children; help maintain better health status; coordinate substance abuse care throughout various institutions and agencies; and tailor care to specific social and medical needs of the woman, her family, and her children. Case management involves all members of the extended family and should include enlisting the positive action of the male partner. Children benefit from such efforts, too. Often children of FAS-producing mothers are in foster placement because of neglect or abuse. A major motivator for maintenance and aftercare is to improve the social and health status of the mother so that she can regain or retain custody of her children.

Recommendations

- The committee recommends that until such time as clear dose-response relationships are established, pregnant women and those abour to become pregnant be counseled to avoid alcohol consumption throughout pregnancy.
- The committee recommends greatly increased attention among sponsors of prevention initiatives, independent of the target population, to evaluating the effectiveness of programs implemented. This recommendation applies to all levels of prevention interventions.
- The committee recommends that research efforts include comparisons of prevention methods at all levels in order to provide information to policy makers about relative costs and benefits.

Indicated Prevention Interventions

- The committee recommends that a high priority be placed on research efforts to design, implement, and evaluate prevention interventions that can effectively guide pregnant women who drink heavily to alcohol treatment. Research or programs should also include:
  - implementation of appropriate screening tools, including biomarkers of alcohol exposure, to identify women who are drinking moderate to heavy amounts of alcohol during pregnancy;
  - assessment of methods to involve women's partners and family members in interventions to decrease or stop drinking;
  - incorporation of comprehensive reproductive counseling and contraceptive services in prevention and treatment programs for substance-abusing women;
  - assessment of the effectiveness and economic benefits of protocols for case management and follow-up of women, and of their families, who have given birth to a child affected by fetal alcohol exposure;
  - development of training programs for professionals in the identification of heavy drinking, and referral to appropriate regional centers or prevention services;
  - use of multiple outcome measures to assess the effectiveness of prevention initiatives; and
  - basic research in animal models to elucidate further the mechanisms of alcohol teratogenesis, which might lead to pharmacologic or other strategies for amelioration of the effects of alcohol exposure in utero.

Selective Prevention Interventions

- The committee recommends increased research efforts to design, implement, and evaluate selective prevention interventions to decrease risks of FAS, ARND, and ARBD through programs aimed toward women who are pregnant or may become pregnant, and who drink alcohol. Designing such interventions will be aided by further research assessing the contribution of personal and socio-environmental risk and protective factors that affect levels of drinking by women during pregnaricy.
- Where the utility of specific intervention programs has been established, the committee recommends broad implementation of successful prevention interventions. Programs developed or studied should include the following:
  - specific demographic groups that have been demonstrated to be at higher risk for FAS, ARBD, and ARND, as well as those who exhibit risk factors associated with moderate to heavy alcohol consumption during pregnancy;
  - implementation of prevention efforts in a wide range of communities and media;

Universal Prevention Interventions

- The committee recommends that although data are insufficient regarding the effectiveness of universal prevention interventions, such interventions should be continued to raise awareness about the risks of FAS, ARBD, and ARND. However, the most important approach to universal prevention is probably the development of a medical environment in which concepts of the risk of FAS, ARBD, and ARND are incorporated into routine health care. Further education efforts to reach children and adults about FAS, ARBD, and ARND through health educational curricula and other means are recommended.

THE AFFECTED INDIVIDUAL

Fetal alcohol syndrome (FAS), alcohol-related birth defects (ARBD), and alcohol-related neurodevelopmental disorder (ARND) are rarely diagnosed. Similarly, although developmental problems in children have been demonstrated through prospective studies to be associated with maternal substance use

(Streissguth et al., 1993), these problems are often not acknowledged except in the most extreme cases. As a result, many affected individuals do not receive correct diagnosis or treatment for their alcohol-related disabilities. There has been a curious lack of enthusiasm for targeted efforts directed at the prevention of secondary disabilities.

Originally, it was not clear which factors produced these poor developmental outcomes--whether, that is, the observed problems resulted from damage to the nervous system or from poor caregiving. However, there are now convergent data from long-term clinical studies of individuals with FAS gathered from number of different populations arguing that outcome can be predicted most effectively by examining the interaction between severity of biological insult (operationally defined as dysmorphia) and environmental risk (operationally defined as caregiving instability and abuse or neglect). In studies of high-risk children in general, poor social and caregiving environments exacerbate negative outcomes, whereas middle-class social status (Aylward, 1992) and well-designed early intervention (Bryant and Ramey, 1987) ameliorate these negative effects. However, few systematic attempts have been made to intervene with alcohol-affected children to test the possibility that such strategies would be effective in producing more positive outcomes.

When considered, the view that intervention may not be useful in children affected by alcohol seems odd, because it is inconsistent with the attitude taken toward other groups of high-risk and disabled children, who are the focus of many early intervention and special education efforts (Meisels and Shonkoff, 1990).

In understanding how to meet the needs of individuals with FAS, it is first necessary to describe the behavioral characteristics of affected children as well as the social environment in which many affected children live. Information about affected children is derived mainly from two sources: (1) retrospective and clinical studies of clinically referred children with FAS and fetal alcohol effects, and (2) prospective research studies of children exposed to alcohol in utero due to maternal drinking. In most such prospective studies, maternal drinking is in the light to moderate range, with only a few women drinking in the heavy range. As a result, most of the children in these prospective studies are not dysmorphic and would not, therefore, qualify for a diagnosis of FAS, although in some cases they may have milder effects that are observable through focused testing or the statistical analysis of group data.

On average, individuals with the full syndrome are mildly mentally retarded, with IQ *scores* in the 60s (Streissguth, 1986). However, there is wide variability in presentation. Individuals with partial FAS, ARBD, or ARND often have IQ scores in the "borderline" range (i.e., 70 to 85), and are frequently described in the scientific literature and popular press as having "normal" intelligence. In fact, having intellectual abilities in this range can be very disabling socially and adaptively, particularly if accompanied by the other kinds of problems often found in children growing up in alcoholic families (Brown, 1991; Sher, 1991).

Behavioral deficits have been described by many clinicians. While such patterns are often reported to be characteristic of affected individuals, they are not always seen. Even some dysmorphic children do not show all of these traits (Coles et al., 1994a,b), and in prospectively followed samples of moderately exposed children, few such problems may be seen (N. Day, personal communication, 1994; Greene et al., 1991; Boyd et al., 1991). Because of the nature of the developmental process, the behavioral, as well as the physical, manifestations of the teratogenic effect can change over time. Such apparent inconsistencies make diagnosis and treatment difficult and often lead observers to suggest that effects are unrelated to prenatal exposure. However, a better understanding of the meaning of the presentation of behavioral symptoms may also provide a key to their nature.

It is frequently difficult in the newborn period to diagnose FAS or ARND because of the lack of development of specific facial features that are often thought to be more recognizable during the preschool period. Trained observers can identify both the facial features and the behavioral signs associated with

prenatal alcohol exposure during this period. Behavioral patterns characteristic of alcohol-exposed neonates are often those associated with withdrawal from a CNS depressant.

Fewer studies have examined effects in the first two years of life and, often. there have been no effects demonstrated, particularly in samples of children without the full syndrome. Growth measures, the metrics of which are more direct and precise than those of behavior, have been found to withstand statistical manipulations sufficiently to allow identification of effects of moderate exposure. Only children who are clearly affected (i.e., dysmorphic or growth retarded) or those who are participating in well-controlled prospective studies (Jacobson et al., 1993) have shown effects on global developmental tests during this period.

In contrast, uhen FAS is identified as clinically significant in infancy and babies are followed medically, there are a number of characteristic problems associated with fetal alcohol exposure, including failure to thrive (often associated with feeding difficulties), delays in development, motor dysfunction, otitis media, *and* cardiac problems. Unfortunately, clinically referred children are often victims of abuse and neglect as well as prenatal exposure and, for that reason, may also suffer from behavioral problems associated with those conditions (e.g., reactive attachment disorder [American Psychiatric Association, 1994] or the behavioral effects of stress), and it can be difficult to discriminate one behavioral effect from another. particularly among individual children in a clinical setting (Zeanah et al., 1993). There are relatively few studies of the pre-school period in prospectively followed alcohol-exposed children. In clinically identified yroups, presentation varies, depending on the child's caregiving environment, as well as other factors. Children of this age have been described both as lively, friendly, and socially interested and also as exhibiting hyperactivity, ADHD, language dysfunction, perceptual problems, and behavioral disturbances.

When descriptions of clinical samples of alcohol-affected children's language problems are examined, there is an apparent discrepancy between the child's vocabulary and fluency and the general ability to communicate effectively. Difficulties appear to involve comprehension and social discourse or the pragmarics of speech.

At school age, clinically referred, affected children are described as unable to sit still in class and pay attention to school work. They are said to find it difficult to deal with multiple sensory inputs, particularly auditory information, and to show significant difficulties in peer relationships and to "lack remorse," to fail to learn from mistakes, to lack judgment, to be unusually aggressive, and to be unable to maintain friendships. There is no research-based information available on social and emotional status or other aspects of development in these children. In prospective studies it is at school age that deficits in cognitive performance begin to appear reliably (Coles et al., 1991a,b; Nanson and Hiscock, 1990), and these have been found even in the absence of physical dysmorphia (Day, personal communication, February 1995; Streissguth et al., 1990).

There are few studies of older school-aged children who have been exposed to alcohol. The only prospective study of mild to moderately exposed children *without* dysmorphia who were followed into later childhood found that measures of "binge" drinking (more than five drinks per occasion) during pregnancy were most highly related to later academic difficulties. These children were described by teachers as distractable, restless, and lacking in persistence in contrast to other children in the sample. They were also identified as having problems with processing and reasoning.

In clinical populations, adolescents and young adults with FAS are considered to have significant deficits in intelligence, learning, academic achievement, and-more particularly-in social behavior. Adaptive behavior and social judgment were more impaired than intellectual functioning In addition, there are grounds for concern that these youth are at much greater risk for substance abuse than others of this age' due to familial exposure and potential effects of their prenatal exposure.

There are little data on adults with FAS. Thus, there is no information about longevity, sexuality, parenting, vulnerability to disease or mental illness, or other data that would be valuable in planning for these individuals. Anecdotal information suggests that the prognosis is poor and includes a higher risk for substance abuse, criminal behavior, deteriorating mental health, and similar problems. However, it is unwise to generalize from such fragmentary information.

For the clinician, as well as the research scientist, there are several important questions that must be answered in order to plan interventions with individuals with FAS, partial FAS and ARND. The first question is whether there are discernible patterns in the development of prenatally exposed children. A review of existing information about the development of these children suggests the following conclusions: *The data base is limited, There is a great deal of variability in outcome, Early identification is possible in some cases, Effects of prenatal exposure appear to become more significant later in the child's development, perhaps due to the nature of a disorder that may affect behaviors associated with more mature social functioning.*

The second significant question is whether developmental problems seen in alcohol-exposed children should be attributed solely to the effects of the teratogen on neurological functioning, solely to the effects of environmental factors such as social class and dysfunctional families, or to some combination of the two. At present, there is no easy answer to this question. The social and environmental factors that may affect their development have not been adequately investigated. Anecdotal evidence suggests that children with FAS, ARBD or ARND are more likely to have negative caregiving environments than are typical children or children with other disabilities. The first risk for these children is loss of their biological parents. Clinical observation also suggests that children with FAS or possible alcohol-related effects often come to the attention of protective service agencies and frequently may enter foster care or be placed for adoption (Table 8-1).

It is not clear that the behaviors reportedly shown by alcohol-affected individuals are different from those shown by other persons who are mentally retarded, have specific learning disabilities, are diagnosed with ADHD, or have been reared in dysfunctional families. It is currently unknown whether the behavior problems reported in children and adolescents (Spohr et al., 1993; Streissguth et al., 1991) with FAS are specific to this group or are common to individuals with complex intellectual deficits.

Although in some cases the prenatal exposure may have had permanent effects, it still might be possible to avoid the development of secondary disabilities in these individuals by early identification and appropriate treatment over the life span. There is no systematically compiled information available describing the number that receive services or the kinds of services received by individuals with FAS or other alcohol-related deficits. Some, although not all, alcohol-affected children qualify for existing early intervention and special education services. At the present time, there are no empirical studies available of the effects of educational intervention, either generalized (the standard services offered to all qualifying children) or specific (programs specifically designed for those with FAS or ARBD), on alcohol-affected children. Faced with a lack of published information about teaching methods and the effectiveness of treatment for alcohol-exposed children, some teachers and parents have turned to the "wisdom of practice". However, to determine whether they are more or less effective with children with fetal alcohol effects, evaluation of methods and programs will be required.

In addition to medical and educational interventions directed at affected individuals, other strategies have been considered to improve outcomes for alcohol-affected children and adults. Because the child is being reared within a family, whether the biological family or an adopiive'or foster family, intervention for the prevention of secondary disabilities in alcohol-affected children must address the needs of the family as well. In dealing with both families who have produced a child with FAS and those caring for ihese children in foster or adoptive situations, it is necessary to examine the extent of coping abilities. Parenting education

can be 'an effective adjunct to other treatments and educational interventions. Support groups have been formed in a number of states, but their effectiveness has not yet been evaluated.

Although many providers are willing to serve children with FAS, sometimes it is difficult to identify individuals accurately. At present, there are no universally applied diagnostic criteria or instrument(s) for the diagnosis of FAS, ARBD, and ARND. Another problem is related to the young child's characteristics and the problem of measurement. From infancy through early school age, cognitive deficits are usually "mild" and motor deficits are relatively subtle compared to those usually treated in early intervention programs. Generally, to receive therapeutic services, children must meet state or district criteria, which usually involve standardized testing. Often, to receive services, infants and preschool children must score less than 70 (2 standard deviations [SD] below the mean) on a standardized test in at least one area of functioning (usually cognitive, motor, or language development) or, in some cases 1.5 SD in two areas. Because alcohol-exposed infants may not score in this deficit range during the first year, many do not qualify for services during that time. However, children with other conditions associated with later deficits (e.g., Down syndrome) may not always score in the deficit range during the first year due to the problem of measurement associated with infant tests. Because the prognosis for children with Down syndrome is well known, however, such children are usually not denied services.

Conclusions and Recommendations

The committee concludes that there are no specific programs to treat children with FAS, ARBD, or ARND, and other efforts to prevent secondary disability in these children are insufficient and inadequate. Given the known value of early intervention, however, it is important to identify children with FAS, ARBD, or ARND as early as possible. Thus, in the committee's view, action to bring needed programs and efforts to an acceptable level must proceed on a number of fronts. For example, as pointed out in other chapters, there is a critical need for more consistent diagnostic criteria and better surveillance. Application of these criteria requires the availability of well-trained professionals in social services, education, and health care, as well as those charged with developing policies that impact services for special children. The committee, therefore, recommends the following actions to address these needs:'

- Clusters of high-quality diagnostic and treatment services should be available locally and regionally.
- Programs that offer training of professionals and that serve as resource centers for schools and medical clinics should be established.
- Programs serving children with FAS, ARND, or ARBD should meet the special, complex needs of such children, including consideration of the families involved and increased availability of parenting training for caretakers (birth parents, foster parents, and adoptive parents).
- Community outreach programs should be available to establish appropriate lines of communication with clinicians, judges, police, psychologists, teachers, and both birth and adoptive/foster parents.
- Educational materials should be developed for professionals who deal with school-age children to increase their awareness of FAS, ARND, or ARBD as a potential cause of ADHD-like behaviors, including hyperactivity, and to facilitate their referral of such children to other appropriate or needed services.
- Ways should. be developed to address the issues of confidentiality that apply to identifying and treating children exposed to alcohol (or other substances) in utero.
- Clinical practice guidelines should be developed for follow-up and treatment of children with FAS, ARND, or ARBD.

A necessary complement to the above actions is an expanded knowledge base. The committee, thus, views further research as essential to providing adequate treatment of children affected by FAS. ARND, and ARBD. The committee recommends additional research in the following areas:

- research to distinguish the role of the postnatal environment in modifying the effects of fetal alcohol exposure, including research on adopted versus nonadopted children with these disorders;
- research on the social and emotional status of school age children affected by FAS, ARND, or ARBD and research on the existence of specific impairments associated with these syndromes, particularly impairments in attention, language, sensory integration, and other behavioral problems;
- further basic research using animal models to examine the underlying neurobiological mechanisms of behavioral and environmental interventions over the life span; and
- evaluation of the effectiveness of educational interventions on children with FAS, ARND, or ARBD, possibly beginning with the examination of educational interventions that look promising in case studies or in studies of children exposed to illicit drugs in utero.

INTEGRATION AND COORDINATION: A CONCLUDING COMMENT AND RECOMMENDATION

There is no single, organized discipline within medicine that can, at this time, logically be held responsible or accountable for the development of a comprehensive approach to preventing and treating fetal alcohol syndrome (FAS), alcohol-related neurodevelopmental disorder (ARND), or alcohol-related birth defects (ARBD). Nor is there a single discipline in the broader arena of health and health care appropriate for this role. The problem is obvious. Primary care health care providers are frequently presented with the opportunity IV detect substance abuse and make referrals for treatment. Psychiatrists and other mental health care workers also are responsible for problems of recognizing and treating addiction. Obstetricians and family physicians are concerned principally with the prevention and management of teratogenic exposures, while pediatricians and family physicians manage birth defects in infants. Because the disorders pose health and developmental problems over the life span, they have been variably managed after the newborn period by pediatric subspecialists such as clinical geneticists, developmentalists, child neurologists, and others. No group has yet shown any interest in the management of FAS, ARBD, or ARND patients as adults. Therefore, these disorders lie within the purview of many groups but are clearly not the full responsibility of any one. All groups will accept, or have accepted, an interest in handling an appropriate piece of the problem, but no one is in a position to lead and coordinate. Hence, there is no group to which government can look for leadership, and no group is focused on advocacy or comprehensive education about the disorders. Attention to FAS, ARBD, and ARND, then, is structurally marginalized, and like any problem that falls between organized disciplines, progress is unavoidably hampered., Both FAS research and service delivery suffers.

Such structural marginalization is also evident in government, where it is difficult to find a government system that is positioned to address these disorders in a comprehensive manner. The National Institute on Alcohol Abuse and Alcoholism (NIAAA) has lead responsibility for research on alcohol and historically has played the major role in FAS research. The Centers for Disease Control and Prevention recently has expanded its FAS activities beyond surveillance into prevention. The Substance Abuse and Mental Health Services Agency (SAMHSA) funds prevention and treatment demonstration projects for substance-abusing pregnant women, including women at risk for having a child with FAS. The Health Services and Resources Administration co-funds some of the SAMHSA programs and sponsors maternal and child health projects. The Indian Health Service provides services to populations at risk for FAS and other

alcohol-related problems. No agency has assumed responsibility for research on interventions with people affected by FAS, ARBD, or ARND. No agency has responsibility for coordinating the many services needed by families affected by FAS and related disorders. It is often difficult to achieve meaningful cooperation among government research and services agencies for a given problem. Such cooperation, however, can be facilitated by willingness of individual personnel to move beyond the structural barriers of government bureaucracies. In most state governments, agencies responsible for child neglect and abuse, foster and adoptive care, health, education, criminal justice, and alcohol treatment are distinct entities. Yet, interagency coordination of personnel and budgets is needed for state governments to help patients and their families affected by FAS, ARND, or ARBD, without involving the criminal justice system or the social service community that is focused on child abuse. At the federal level, there is similarly no single agency responsible for all the programs or research needed.

It is clear that neither governmental structures nor the organization of modern medicine and health care can be redesigned. Thus, the challenge is to improve communication and cooperation among health, education, and social services disciplines and government agencies. The committee believes that such cooperation among medical disciplines may best be addressed by the recommendations made to increase professional education about FAS and its related disorders, and to establish clinical practice guidelines for the management of patients and their families. Further, the committee believes that any possible coordination at a state level will depend first on leadership shown by federal agencies to communicate with each other and to coordinate programmatic goals and objectives.

Therefore, the committee recommends that an interagency task force, or other entity comprised of representatives from the relevant federal research, surveillance, and services agencies, be established to coordinate national efforts in FAS, ARND, and ARBD. Lead responsibility for heading this task force should be assigned to NIAAA, because it is experienced at encouraging research and at incorporating research methodologies into all activities and has had the longest history in addressing FAS. However, all member agencies should be willing and able to translate research findings into service delivery and policy development activities and be expected to contribute to and be consulted with about achieving the overall goals of preventing FAS. It is suggested that one of the top priorities of such a coordinating body should be to forge interagency cooperation in the adoption of a common terminology and set of definitions related to these disorders, such as proposed in this report, and the design and implementation of national surveys to estimate the true prevalence of FAS, ARND, and ARBD. At the same time, prevention and treatment of secondary disabilities associated with FAS. ARND, and ARBD, as well as prevention and treatment of alcohol abuse and dependence by pregnant women and by women at risk of becoming pregnant, should be a high, and long-term, priority of this coordinating body. Additional important areas of focus should include consideration of basic research and communication among the basic and clinical research communities and the health services community. Recommendations for research in all aspects of FAS can be found in this report and should serve as guidance for the coordinating body. Finally, the coordinating body should take active steps to encourage and facilitate the rigorous evaluation of all intervention programs.

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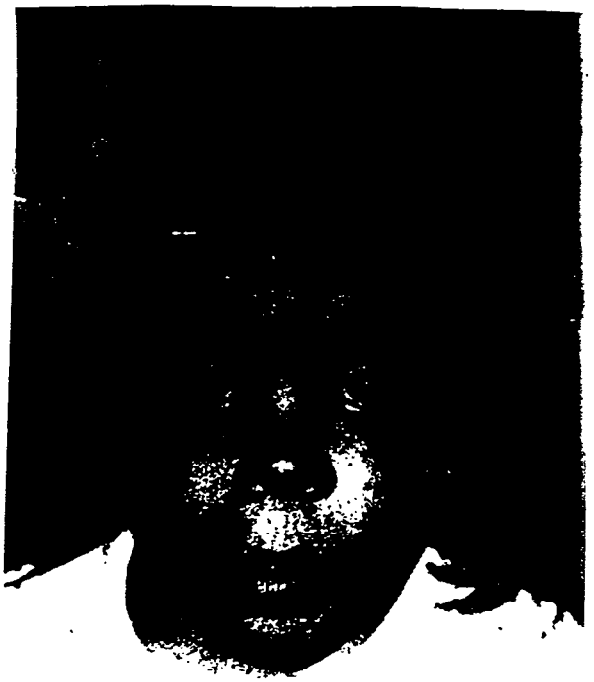
Figure /-/

B.



C.

D.

TABLE 1-1. Examples of Healthy People 2000 Goals Relevant to FAS

Objective	1987 baseline	Target 2000
FAS (per 1,000 live births)	0.22	0.12
Abstinence from alcohol during pregnancy	79%	Increase by 20%
Screening by Obstetrician/Gynecologist for alcohol use	34%	75%
Referrals by Obstetrician/Gynecologist for alcohol treatment	24%	75%
Screening by Obstetrician/Gynecologist for drug use	32%	75%
Referrals by Obstetrician/Gynecologist for drug treatment	28%	75%

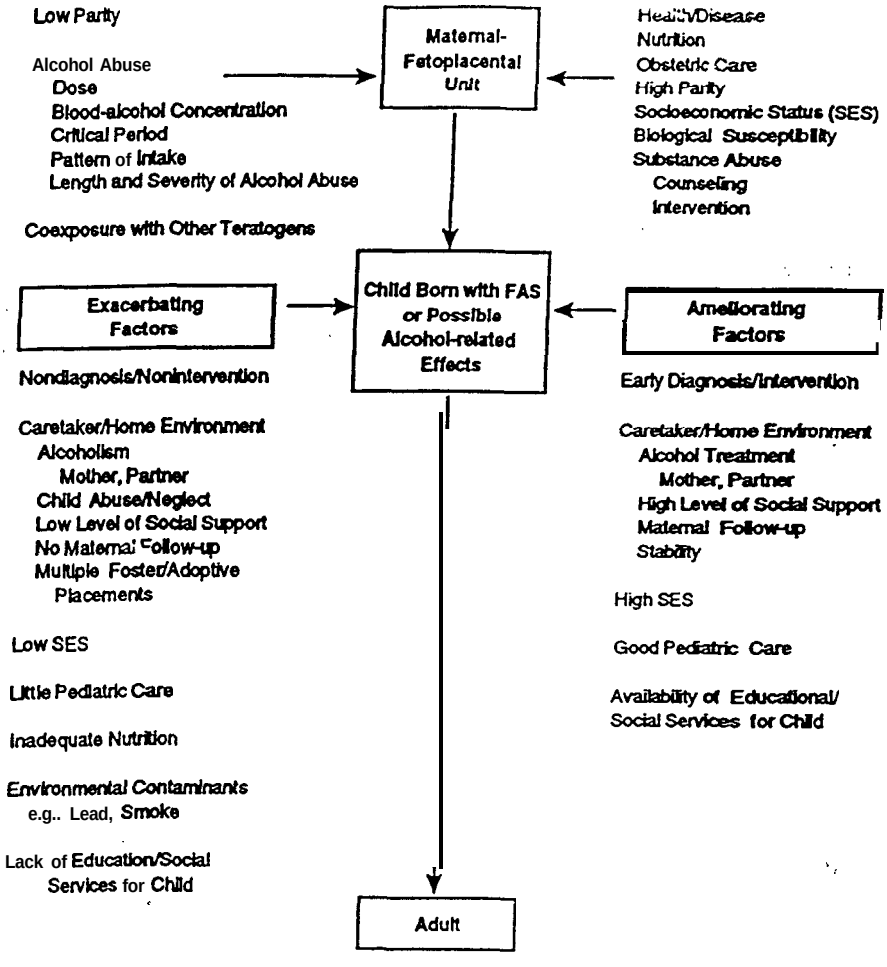


Figure 2-2 Theoretical Influences on the Expression of Prenatal Alcohol Exposure.

TABLE 4-1 DIAGNOSTIC CRITERIA FOR FAS and ALCOHOL-RELATED EFFECTS

FETAL ALCOHOL SYNDROME

1. FAS with confirmed maternal alcohol exposure"

A. Confirmed maternal alcohol exposure[a]

B. Evidence of a characteristic pattern of facial anomalies that includes features such as short palpebral fissures and abnormalities in the premaxillary zone (e.g., flat upper lip, flattened philtrum, and flat midface)

C. Evidence of growth retardation, as in at least one of the following:
- low birth weight for gestational age
- decelerating weight over time not due to nutrition
- disproportional low weight to height

D. Evidence of CNS neurodevelopmental abnormalities, as in at least one of the following:
- decreased cranial size at birth
- structural brain abnormalities (e.g. microcephaly, partial or complete agenesis of the corpus callosum, cerebellar hypoplasia)
- neurological hard or soft signs (as age appropriate), such as impaired fine motor skills, neurosensory hearing loss, poor tandem gait, poor eye-hand coordination

. FAS without confirmed maternal alcohol exposure

, C, and D as above

, Partial FAS with confirmed maternal alcohol exposure

. Confirmed maternal alcohol exposure[a]

B. Evidence of some components of the pattern of characteristic facial anomalies

ither C or D or E

. Evidence' of growth retardation, as in at least one of the following:
- low birth weight for gestational age
- decelerating weight over time not due to nutrition
- disproportional low weight to height

. Evidence of CNS neurodevelopmental abnormalities, as in:
- decreased crania1 size at birth
- structural brain abnormalities (e.g. microcephaly, partial or complete agenesis of the corpus callosum, cerebellar hypoplasia)
- neurological hard or soft signs (as age appropriate) such as impaired fine motor skills, neurosensory hearing loss, poor tandem gait, poor eye-hand coordination

E. Evidence of a complex pattern of behavior or cognitive abnormalities that are inconsistent with developmental level and cannot be explained by familial background or environment alone, such as learning difficulties, deficits in school performance; poor impulse control; problems in social perception; deficits in higher level receptive and expressive language; poor capacity for abstraction or metacognition; specific deficits in mathematical skills; or problems in memory, attention, or judgment

ALCOHOL-RELATED EFFECTS

Clinical conditions in which there is a history of maternal alcohol exposure,[a,b] and where clinical or anima research has linked maternal alcohol ingestion to an observed outcome. There are two categories, which ma co-occur. If both diagnoses are present, then both diagnoses should be rendered:

4. Alcohol-related birth defects (ARBD)

List of congenital anomalies, including malformations and dysplasias

Cardiac	Atrial septal defects Ventricular septal defects	Aberrant great vessels Tetralogy of Fallot
Skeletal	Hypoplastic nails Shortened fifth digits Radioulnar synostosis Flexion contractures Camptodactyly	Clinodactyly Pectus excavatum and carinatum Klippel-Feil syndrome Hemivertebrae Scoliosis
Renal	Aplastic, dysplastic, hypoplastic kidneys Horseshoe kidneys	Ureteral duplications Hydronephrosis
Ocular	Strabismus Retinal vascular anomalies	Refractive problems secondary to small globes
Auditory	Conductive hearing loss	Neurosensory hearing loss
Other	Virtually every malformation has been described in some patient with FAS. The etiologic specificity of most of these anomalies to alcohol teratogenesis remains uncertain.	

Alcohol-related neurodevelopmental disorder (ARND)

resence of

. Evidence 'of CNS neurodevelopmental abnormalities, as in any one of the following:

1. decreased cranial size at birth
2. structural abnormalities such as microcephaly, abnormalities in the development of the corpus callosum
3. 'neurological signs such as impaired fine motor skills, neurosensory hearing loss, poor tandem gait, poor eye-hand coordination

id/or

B. Evidence of a complex pattern of behavior or cognitive abnormalities that are inconsistent with developmental level and cannot be explained by familial background or environment alone, such as learning difficulties; deficits in school performance; poor impulse control; problems in social perception; deficits in higher level receptive, and expressive language; poor capacity for abstraction or metacognition; specific deficits in mathematical, skills; or problems in memory, attention, or judgment

A pattern of excessive intake characterized by substantial, regular intake or heavy episodic drinking. Evidence of this pattern may include frequent episodes of intoxication, development of tolerance or withdrawal. social problems related to drinking, legal problems related to drinking, gaging in physically hazardous behavior while drinking, or alcohol-related medical problems such as hepatic disease.

As further research is completed and as, or if, lower quantities or variable patterns of alcohol use are associated with ARBD or ARND, these tterns of alcohol use should bc incorporated into the diagnostic criteria.

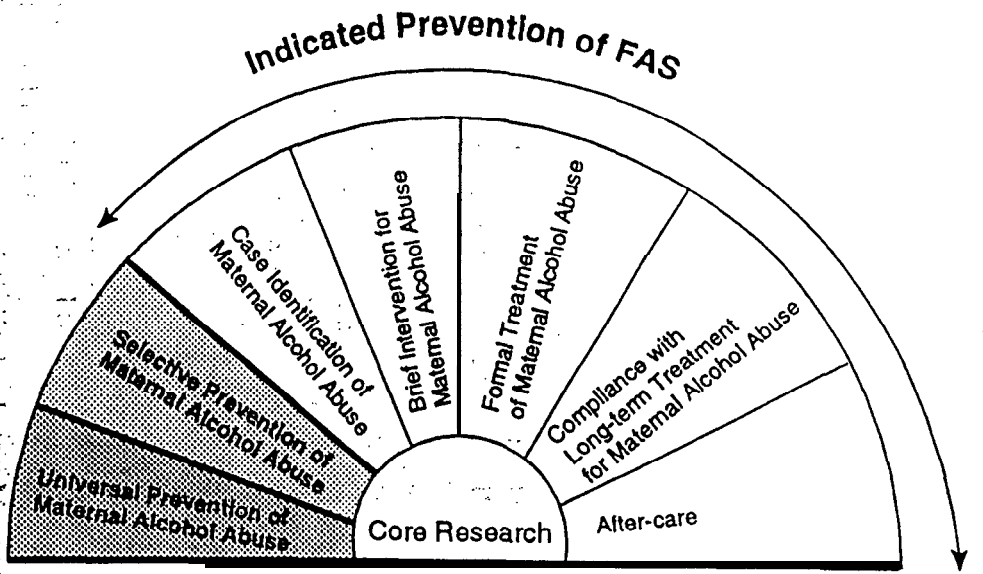


Figure 7-1 **The intervention spectrum for Fetal Alcohol Syndrome. Adapted from Institute of Medicine, 1994.**

BOX 7-6

TWEAK TEST

T *Tolerance:* How many drinks can you hold?

W Have close friends or relatives *Worried* or complained about your drinking in the past year?

E *Eye-Opener:* Do you sometimes take a drink in the morning when you first get up?

A *Amnesia:* Has a friend or family member ever told you about things you said or did while you were drinking that you could not remember?

K(C) Do you sometimes feel the need to Cut *Down* on your drinking?

A 7-point scale is used to score the test. The Tolerance question scores 2 pdints if the responding reports the ability to hold more than five drinks without falling asleep or passing out. A positive response to the Worry question scores 2 points, and a positive response to the last three questions scores 1 point each. A total of 2 or more points indicates the respondent is likely to be **a'** risk drinker.

SOURCE: Russell M. New assessment tools for risk drinking during pregnancy. Alcohol Health and Research World 1994; 18:55-61.